UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

March 22, 2004

MEMORANDUM

Subject: Efficacy Review for EPA Reg. No.: 1839-95, NP 4.5 (D&F) Detergent/Disinfectant; DP Barcode: 297938

From: Tajah Blackburn, Ph.D., Microbiologist
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Applicant: Stephan Company
22 West Frontage Road
Northfield, IL 60093

Formulation from Label:

Active Ingredient(s)	% by wt
Alkyl (60% C_{14}, 30% C_{16}, 5% C_{12}, 5% C_{18}) dimethyl benzyl ammonium chlorides	2.25%
Alkyl (68% C_{12}, 32% C_{14}) dimethyl ethylbenzyl ammonium chlorides	2.25%
Inert ingredient(s)	95.50%
Total	100.00%

I BACKGROUND

The product, NP 4.5 (D&F) Detergent/Disinfectant (EPA Reg. No. 1839-95), is a registered disinfectant (bactericide, virucide, fungicide) and mildewstat for use on hard, non-porous surfaces in household, institutional, industrial, commercial, animal care, and hospital or medical environments. The label claims that the product is effective in the presence of 5% organic soil concentration. The applicant requested an amendment to the registration to add claims for effectiveness against the Human Coronavirus. The study was conducted at ATS LABS, located at 2540 Executive Drive, St. Paul, MN 55120.

The data package contained a letter from the applicant to EPA (dated September 11, 2003), one study (MRID No. 461551-01), a Statement of No Data Confidentiality Claims for the study, and the proposed label.

II USE DIRECTIONS

The product is designed to be used for disinfecting hard, non-porous surfaces such as floors, walls, metal surfaces, stainless steel surfaces, glazed porcelain, glazed ceramic tile, plastic surfaces, vanity tops, shower stalls, bathtubs, and cabinets. Directions on the proposed label provided the following information regarding preparation and use of the product as a disinfectant: Add 2 ounces of the product per gallon of water (1:64 dilution). Apply the use solution with a mop, cloth, sponge, or sprayer. Wet all surfaces for 10 minutes. Remove excess liquid. For heavily soiled areas, a pre-cleaning step is required.

Finally, the proposed label directions note that: "This product is not to be used as a terminal sterilant/high level disinfectant on any surface or instrument that . . . ."

III AGENCY STANDARDS FOR PROPOSED CLAIMS

Virucides

The effectiveness of virucides against specific viruses must be supported by efficacy data that simulates, to the extent possible in the laboratory, the conditions under which the product is intended to be used. Carrier methods that are modifications of either the AOAC Use-Dilution Method (for liquid disinfectants) or the AOAC Germicidal Spray Products as Disinfectants Method (for spray disinfectants) must be used in developing data for virucides intended for use upon dry inanimate, environmental surfaces (e.g., floors, tables, cleaned dried medical equipment surfaces). To simulate in-use conditions, the specific virus to be treated must be inoculated onto hard surfaces, allowed to dry, and then treated with the product according to the directions for use on the product label. One surface for each of 2 different batches of disinfectant must be tested against a recoverable virus titer of at least 10^4 from the test surface for a specified exposure period at room temperature. Then, the virus must be assayed by an appropriate virological technique, using a minimum of four determinations per each dilution assayed. Separate studies are required for each virus. The calculated viral titers must be reported with the test results. For the data to be considered acceptable, results must demonstrate complete inactivation of the virus at all dilutions. When cytotoxicity is evident, at least a 3-log reduction in titer must be demonstrated beyond the cytotoxic level. These Agency standards are presented in DIS/TSS-7.

Supplemental Claims

An antimicrobial agent identified as a "one-step" cleaner-disinfectant, cleaner-sanitizer, or one intended to be effective in the presence of organic soil must be tested for efficacy with an appropriate organic soil load, such as 5 percent serum. These Agency standards are presented in DIS/TSS-2.

IV COMMENTS ON THE SUBMITTED EFFICACY STUDY

1. MRID 461551-01 "Virucidal Efficacy of a Disinfectant for Use on Inanimate Environmental Surfaces, Virus: Human Coronavirus" for NP 4.5 (D&F) Detergent/Disinfectant, by Karen M. Ramm. Study conducted at ATS LABS. Study completion date – May 20, 2003.

This study was conducted against the Human Coronavirus (Strain 229E; ATCC VR-740), using MRC-5 cells (human embryonic lung; obtained from ViroMed Laboratories, Inc., Minneapolis, MN) as the host system. Two lots (Lot Nos. 2536-43 and 2536-44) of the product, NP 4.5 (D&F) Detergent/Disinfectant, were tested according to ATS LABS Protocol No. STE01041603.HCOR.1 (copy not provided). The stock virus culture contained a 5% organic soil load (fetal bovine serum). A use solution was prepared by adding 1 mL of the product to 63 mL of filter sterilized de-ionized water (a 1:64 dilution). Films of virus were prepared by spreading 0.2 mL of virus inoculum uniformly over the bottoms of separate sterile glass Petri dishes. The virus films were dried at 20.1°C for 20 minutes in a relative humidity of 34%. For each lot of product, separate dried virus films were exposed to 2.0 mL of the use solution for 10 minutes at 20±1°C. After exposure, the plates were scraped with a cell scraper to re-suspend the contents, passed through a Sephadex column, and diluted serially in Eagle's minimal essential medium supplemented with 2% heat-inactivated fetal bovine serum, 10 µg/mL gentamicin, 100 units/mL penicillin, and 2.5 µg/mL amphotericin B. MRC-5 cells in multi-well culture dishes were inoculated in quadruplicate with 0.1 mL of the dilutions. The cultures were incubated at 31-35°C in a humidified atmosphere of 5-7% CO_2 and scored periodically for 7 days for the presence or absence of unspecified cytopathic effects, cytotoxicity, and viability. Controls included cytotoxicity, dried virus controls, and neutralization. Viral and cytotoxicity titers were calculated by the method of Spearman Karber.

V RESULTS

MRID Number	Organism	Results			Dried Virus Control ($TCID_{50}$/0.1 mL)
			Lot No. 2536-43	Lot No. 2536-44	
461551-01	Human Coronavirus	10^{-1}	Cytotoxicity	Cytotoxicity	$10^{4.5}$
		10^{-2} to 10^{-7} dilutions	Complete inactivation	Complete inactivation	
		$TCID_{50}$/0.1 mL	$\leq 10^{1.5}$	$\leq 10^{1.5}$	
		Log reduction	≥ 3.0 $\log_{10}$	≥ 3.0 $\log_{10}$	

VI CONCLUSION

1. The submitted efficacy data (MRID No. 461551-01) support the use of the product, NP 4.5 (D&F) Detergent/Disinfectant, as a disinfectant with virucidal activity against the Human Coronavirus on hard, non-porous surfaces in the presence of a 5% organic soil load (fetal bovine serum) for a contact time of 10 minutes at a 1:64 dilution. Cytotoxicity was observed in the 10^{-1} dilution. Complete inactivation (no growth) was indicated in the 10^{-2} through 10^{-7} dilutions. A log reduction of $\geq$3.0 was reported. A recoverable virus titer of at least 10^{4} was achieved.

VII RECOMMENDATIONS

1. The proposed label claims (as supported by MRID No. 461551-01) are acceptable regarding the use of the product, NP 4.5 (D&F) Detergent/Disinfectant, as a disinfectant on hard, non-porous surfaces against the Human Coronavirus for a contact time of 10 minutes in the presence of a 5% organic soil load at a 1:64 dilution.

2. The proposed label now includes references for using the product for sanitation (e.g., see marketing language on page 1 "Formulated for Effective Farm Premise Sanitation"). The label does not include any specific instructions for using the product as a sanitizer.

3. The proposed label indicates that the product may be used on fiberglass surfaces [see pages 2 and 3 of the proposed label]. Fiberglass is a porous surface. The applicant must delete this general reference to fiberglass. The applicant may indicate on the product label that the product may be used on specific fiberglass surfaces (e.g., fiberglass bathtubs).

4. The proposed label indicates that the product may be used on picnic tables and outdoor furniture [see page 2 of the proposed label]. Some picnic tables and outdoor furniture are porous. The applicant must delete this general reference, and specify the type of picnic and furniture surfaces.

5. The proposed label indicates that the product may be used on shower curtains [see page 2 of proposed label]. The applicant must delete this general reference, and specify the types of shower curtains for which the product may be used.

6. The proposed label indicates that the product may be used on ear muff and hearing protectors. Both of these use sites may be porous. The applicant must delete this general reference, and specify the type of ear muffs and protectors for which the product may be used.

7. The proposed label [see page 4 of the proposed label] includes *"Trichophyton mentagrophytes"* and after the listed organism, "Athlete's foot fungus." Athlete's foot fungus is caused by several different fungi, therefore it is more accurate to state that it is "a causative agent" of Athlete's foot.

8. The proposed label now includes a section entitled "Poultry (and Swine) Premise Sanitation" [see page 5 of the proposed label]. The applicant should change "Poultry (and Swine) Premise Sanitation" to read "Poultry (and Swine) Premise Disinfection." The product is a disinfectant.

9. A contact time of 60 seconds is specified in the "Shoe Bath Directions" [see page 6 of the proposed label]. Disinfectant directions on the proposed label specify a 10 minute contact time. The applicant should revise the contact time to read "10 minutes."

10. On page 7 of the proposed label, under the section "For rotary floor machines:, the applicant should revise the following sentence because the meaning is unclear: "Follow the cleaning procedures specifically the manufacturer of the cleaning equipment."

11. The applicant may want to make the following changes to the proposed label:

- On page 2, change "refrigerators exteriors" to read "refrigerator exteriors."
- On page 3, change "walls floors of coolers" to read "walls and floors of coolers."
- On page 5, change "feeding end watering appliances" to read "feeding and watering appliances."
- On page 6, change "breath this fog" to read "breathe this fog."
- On page 6, change "Remove all litter, droppings, and manure from floors. Walls and surfaces . . . ." to read "Remove all litter, droppings, and manure from floors, walls, and surfaces . . . ."
- On page 6, change "Thoroughly scrub all treated feed racks, managers, troughs . . ." to read "Thoroughly scrub all treated feed racks, mangers, troughs . . ."
- On page 6, change "In" to "in" in the Directions for Hatchery Rooms Using Fogging Devices section.
- On page 7, change ". . . and apply at he rate of 300-500 . . ." to read ". . . and apply at the rate of 300-500 . . ."